TFW

1645

AMENDMENT TRANSMITTAL LETTER

Docket No. C1039.70020US00

Application No.	Filing Date	Examiner	Art Unit
09/337584-Conf. #9169	June 21, 1999	N. M. Minnifield	1645

Applicant(s): Arthur M. Krieg et al.

Invention: IMMUNOSTIMULATORY NUCLEIC ACID MOLECULES

TO THE COMMISSIONER FOR PATENTS

Transmitted herewith is an Interference Suggestion Pursuant to 37 C.F.R. § 41.202 in the above-identified application.

The fee has been calculated and is transmitted as shown below.

CLAIMS AS AMENDED					
	Claims Remaining After Amendment	Highest Number Previously Paid	Number Extra Claims Present	Rate	
Total Claims		- 20 =		x	
Independent Claims		- 3 =		x	
Multiple Dependent Claims (check if applicable)	☐				
Other fee (please specify):					
TOTAL ADDITIONAL FEE FOR THIS AMENDMENT:					0.00

☒ Large Entity ☐ Small Entity

☒ No additional fee is required for this amendment.

☐ Please charge Deposit Account No. _____ in the amount of $ _____. A duplicate copy of this sheet is enclosed.

☐ A check in the amount of $ _____ to cover the filing fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☒ The Director is hereby authorized to charge and credit Deposit Account No. 23/2825 as described below. A duplicate copy of this sheet is enclosed.

☒ Credit any overpayment.

☒ Charge any additional filing or application processing fees required under 37 CFR 1.16 and 1.17.

Helen C. Lockhart

Dated: August 25, 2006

Helen C. Lockhart
Attorney/Agent Reg. No.: 39,248

WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
(617) 646-8000

Certificate of Mailing Under 37 CFR 1.8(a)

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: August 25, 2006 Signature: Sharon R. Lloyd (Sharon R. Lloyd)

DOCKET NO.: C1039.70020US00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Arthur M. Krieg et al.
Serial No.:	09/337,584
Confirmation No.:	9619
Filed:	June 21, 1999
For:	IMMUNOSTIMULATORY NUCLEIC ACID MOLECULES
Examiner:	Nita Minnifield
Art Unit:	1645

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to MAIL STOP AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the 25th day of August, 2006.

Sharon R. Lloyd

MAIL STOP AMENDMENT
Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Interference Suggestion Pursuant to 37 C.F.R. § 41.202

Applicant hereby requests that an interference be declared between the above-identified application and US 6,498,148 B1. Pursuant to 37 C.F.R. § 41.202(a), the following information is provided.

41.202(a)(1) - Identify the patent with which the applicant seeks an interference

The patent with which Applicant seeks an interference is US 6,498,148 B1, filed on January 21, 1999; claiming priority to US 08/927,120, filed September 5, 1997; and issued to Eyal Raz on December 24, 2002.

41.202(a)(2)(a) - Interfering claims

At least claims 1 and 17 of US 6,498,148 interfere with Applicant's pending claim 44.

41.202(a)(2)(b) - Proposed count

Applicant proposes the following count:

Count 1

Claim 17 of US 6,498,148 or Claim 44 of US 09/337,584

41.202(a)(2)(c) - Correspondence of claims and the count

Claims 1-4 and 6-19 of US 6,498,148 and claims 42-45, 47, 49-53, 57, 90, 92, 94, 96, 98, 100, 102 and 103 of '584 application correspond to the count.

Claims of US 6,498,148	**Correspondence to Count**
1. A method for treating asthma, comprising: administering to a mammal sensitized to an asthma-stimulating antigen an immunostimulatory polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the sequence 5'-cytosine-guanine-3', wherein the immunostimulatory polynucleotide does not comprise a nucleotide sequence encoding the antigen, and wherein the immunostimulatory polynucleotide is administered without the antigen, including without a polynucleotide encoding the antigen, and in an amount sufficient to treat asthma.	Anticipated by the count.
2. The method of claim 1, wherein the ISS comprises the sequence 5'-purine-purine-cytosine-guanine-pyrimidine-pyrimidine-3'.	Obvious over the count in view of sequences disclosed in US 6,194,388, e.g., see, Col. 10, lines 27-29 and Table 1.
3. The method of claim 2, wherein the ISS comprises the sequence 5'-AACGTT-3'.	Obvious over the count in view of sequences disclosed in US 6,194,388, e.g., see Col. 10, lines 38-41 and Table 1.

4. The method of claim 2, wherein the ISS comprises a nucleotide sequence selected from the group consisting of AGCGTC, GACGTT, GGCGTT, AACGTC, GACGTC, GGCGTC, AGCGCC, GACGCC, GGCGCC, AGCGCT, GACGCT, GGCGCT, AACGCT, AACGTT, AGCGTT, and AACGCC.	Obvious over the count in view of sequences disclosed in US 6,194,388, e.g., see Col. 8, lines 17-20, and Col. 10, lines 27-29 and 58-41 and Table 1.
6. The method of claim 2, wherein the ISS comprises a nucleotide sequence selected from the group consisting of AGCGUC, GACGUU, GGCGUU, AACGUC, GACGUC, GGCGUC, AGCGCC, GACGCC, GGCGCC, AGCGCU, GACGCU, GGCGCU, AACGCU, AACGUU, AGCGUU, AACGCC, GACGUT, GACGTU, GGCGUT, GGCGTU, AACGUT, AACGTU, AGCGUT, and AGCGTU.	Obvious over the count in view of sequences disclosed in US 6,194,388, e.g., see, Col. 10, lines 27-29 and Col. 7, lines 37-42.
7. The method of claim 1, wherein the immunostimulatory polynucleotide is administered intramuscularly.	Obvious over the count in view of administration methods disclosed in US 6,194,388, e.g., Col. 18, lines 35-44 and knowledge of person skilled in the art.
8. The method of claim 1, wherein the immunostimulatory polynucleotide is administered to skin.	Obvious over the count in view of administration methods disclosed in US 6,194,388, e.g., Col. 18, lines 35-44.
9. The method of claim 1, wherein the immunostimulatory polynucleotide is administered to respiratory tissue.	Obvious over the count in view of administration methods disclosed in US 6,194,388, e.g., Col. 18, lines 35-44 and knowledge of person skilled in the art.
10. The method of claim 1, wherein the immunostimulatory polynucleotide is linked to a peptide, wherein said peptide is not the antigen to which the mammal is sensitized.	Obvious over the count in view of nucleic acid delivery complexes disclosed in US 6,194,388, e.g., Col. 8, line 58 to Col. 9, line 6 and knowledge of person skilled in the art.
11. The method of claim 10, wherein the peptide is a targeting moiety.	Obvious over the count in view of nucleic acid delivery complexes disclosed in US 6,194,388, e.g., Col. 8, line 58 to Col. 9, line 6 and knowledge of person skilled in the art.

12. The method of claim 10, wherein the peptide is a cytokine.	Obvious over the count in view of nucleic acid delivery complexes disclosed in US 6,194,388, e.g., Col. 8, line 58 to Col. 9, line 6 and knowledge of person skilled in the art.
13. The method of claim 1, wherein the immunostimulatory polynucleotide is linked to an antibody.	Obvious over the count in view of nucleic acid delivery complexes disclosed in US 6,194,388, e.g., Col. 8, line 58 to Col. 9, line 6 and knowledge of person skilled in the art.
14. The method of claim 1, further comprising administering an immunotherapeutic agent.	Obvious over the count in view of coadministration of vaccines disclosed in US 6,194,388, e.g., Col. 17, line 65 to Col. 18, line 9.
15. The method of claim 1, further comprising administering an anti-inflammatory agent.	Obvious over the count in view of knowledge of person skilled in the art.
16. The method of claim 1, wherein eosinophil accumulation in lung tissue is reduced.	Inherent in count and obvious over the count in view of reduction in lung accumulation of eosinophils disclosed in US 6,207,646, e.g., Example 12.
18. The method of claim 1, wherein inflammation stimulated by the asthma-stimulating antigen is reduced.	Inherent in count and obvious over the count in view of reduction of inflammatory response disclosed in US 6,207,646, e.g., Example 12.
19. The method of any one of claim 1, 2, 3, 4, 5, or 17, wherein the mammal is a human.	Obvious over the count in view of human subjects disclosed in US 6,194,388, e.g., Col. 9, lines 23-25.

Claims of US 09/337,584	Correspondence to Count
42. A method for treating asthma in a subject, comprising administering to an asthmatic subject an effective amount for treating asthma in the subject of an immunostimulatory nucleic acid, having a sequence including at least the following formula: 5' X_1 X_2CGX_3 X_4 3' wherein C is unmethylated, wherein X_1X_2 and X_3X_4 are nucleotides, wherein at least one internucleotide linkage has a phosphate backbone modification.	Obvious over the count in view of phosphate backbone modified oligonucleotides disclosed in US 6,194,388, e.g., claim 8.
43. The method of claim 42, wherein the 5' X_1 X_2CGX_3 X_4 3' sequence is a non-palindromic sequence.	Obvious over the count in view of sequences disclosed in US 6,194,388, e.g., see Table 1.
45. The method of claim 42, wherein the phosphate backbone modification is a phosphorothioate modification.	Obvious over the count in view of phosphorothioate modified oligonucleotides disclosed in US 6,194,388, e.g., claim 9.
47. The method of claim 42, wherein the phosphate backbone modification is a phosphorodithioate modification.	Obvious over the count in view of use of phosphorodithioate backbone modifications known in the art, e.g., in antisense applications.
49. The method of claim 42, wherein X_1X_2 are GpA and X_3X_4 are TpT.	Obvious over the count in view of sequences disclosed in US 6,194,388, e.g., see Col. 8, lines 17-20, Col. 10, lines 27-29 and Table 1.
50. The method of claim 42, wherein X_1 and X_2 are purines and X_3 and X_4 are pyrimidines.	Obvious over the count in view of sequences disclosed in US 6,194,388, e.g., see Col. 10, lines 27-29 and Table 1.
51. The method of claim 42, wherein X_1X_2 are GpA and X_3 and X_4 are pyrimidines.	Obvious over the count in view of sequences disclosed in US 6,194,388, e.g., see Col. 8, lines 17-20, Col. 10, lines 27-29 and Table 1.
52. The method of claim 42, wherein the immunostimulatory nucleic acid is 8 to 40 nucleotides in length.	Obvious over the count in view of sequences disclosed in US 6,194,388, e.g., see Col. 6, lines 18-20.

53. The method of claim 42, wherein the immunostimulatory nucleic acid is an isolated immunostimulatory nucleic acid.	Obvious over the count in view of knowledge of person skilled in the art.
57. The method of claim 42, wherein the immunostimulatory nucleic acid comprises a nucleotide sequence selected from the group of the following nucleotide sequences TCCATAACGTTCCTGATGCT (SEQ ID NO:3), TCCATGTCGTTCCTGATGCT (SEQ ID NO:38), and TCCATGACGTTCCTGATGCT (SEQ ID NO:7).	Obvious over the count in view of sequences disclosed in US 6,194,388, e.g., SEQ ID NO:21.
90. A method for treating asthma in a subject, comprising administering to an asthmatic subject an effective amount for treating asthma in the subject of a nucleic acid, having a sequence including at least the following formula: 5' X_1 X_2CGX_3 X_4 3' wherein C is unmethylated, wherein X_1X_2 and X_3X_4 are nucleotides, wherein at least one internucleotide linkage has a phosphate backbone modification and wherein the nucleic acid has a length of 8 to 40 nucleotides.	Obvious over the count in view of phosphate backbone modified oligonucleotides disclosed in US 6,194,388, e.g., claim 8, and in view of sequences disclosed in US 6,194,388, e.g., see Col. 6, lines 18-20.
92. A method for treating asthma in a subject, comprising orally administering to an asthmatic subject an effective amount for treating asthma in the subject of a nucleic acid having a sequence including at least the following formula: 5' X_1 X_2CGX_3 X_4 3' wherein C is unmethylated, and wherein X_1X_2 and X_3X_4 are nucleotides.	Obvious over the count in view of administration methods disclosed in US 6,194,388, e.g., Col. 18, lines 35-44.

94. A method for treating asthma in a subject, comprising administering to an asthmatic subject an effective amount for treating asthma in the subject of a nucleic acid having a sequence including at least the following formula: 5' X_1 X_2CGX_3 X_4 3' wherein C is unmethylated, wherein X_1X_2 and X_3X_4 are nucleotides, and wherein the nucleic acid is administered by a route selected from the group consisting of transdermal and subcutaneous.	Obvious over the count in view of administration methods disclosed in US 6,194,388, e.g., Col. 18, lines 35-44.
96. A method for treating asthma in a subject, comprising administering to an asthmatic subject an effective amount for treating asthma in the subject of a nucleic acid having a sequence including at least the following formula: 5' X_1 X_2CGX_3 X_4 3' wherein C is unmethylated, wherein X_1X_2 and X_3X_4 are nucleotides, and wherein the nucleic acid is administered in a formulation selected from the group consisting of a nucleic acid delivery complex, a liposome, a virosome, and a nanoparticle.	Obvious over the count in view of nucleic acid delivery complexes disclosed in US 6,194,388, e.g., Col. 8, line 58 to Col. 9, line 6.
98. The method of claim 42, wherein the nucleic acid is administered by a route selected from the group consisting of oral, transdermal, and subcutaneous.	Obvious over the count in view of administration methods disclosed in US 6,194,388, e.g., Col. 18, lines 35-44.
100. The method of claim 42, wherein the nucleic acid is delivered in a formulation selected from the group consisting of a nucleic acid delivery complex, a liposome, a virosome, and a nanoparticle.	Obvious over the count in view of nucleic acid delivery complexes disclosed in US 6,194,388, e.g., Col. 8, line 58 to Col. 9, line 6.
102. The method of claim 44, wherein at least one internucleotide linkage of the nucleic acid has a phosphate backbone modification.	Obvious over the count in view of phosphate backbone modified oligonucleotides disclosed in US 6,194,388, e.g., claim 8.

103. The method of claim 44, wherein the phosphate backbone modification is a phosphorothioate modification.	Obvious over the count in view of phosphorothioate modified oligonucleotides disclosed in US 6,194,388, e.g., claim 9.

41.202(a)(3)(a) - Claim chart to compare claims of patent and application

Claim 17 of US 6,498,148 is presented as claim 1 plus the additional limitation of claim 17 (see bottom of left column of the claim chart).

Claim 17 of US 6,498,148	Claim 44 of US 09/337,584
A method for treating asthma, comprising:	A method for treating asthma in a subject, comprising
administering to a mammal sensitized to an asthma-stimulating antigen	administering to an asthmatic subject [*see * below*]
an immunostimulatory polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the sequence 5'-cytosine-guanine-3',	an immunostimulatory nucleic acid, having a sequence including at least the following formula: 5' X_1 X_2CGX_3 X_4 3' wherein C is unmethylated, wherein X_1X_2 and X_3X_4 are nucleotides,
wherein the immunostimulatory polynucleotide does not comprise a nucleotide sequence encoding the antigen,	[*inherent in claim 44*]
and wherein the immunostimulatory polynucleotide is administered without the antigen, including without a polynucleotide encoding the antigen,	[*inherent in claim 44*]
and in an amount sufficient to treat asthma.	an effective amount for treating asthma in the subject of [*in claim as pending, this phrase located at * above*]
[*from claim 17*]: wherein the ISS is at least six nucleotides in length.	wherein the nucleic acid has a length of 8 to 100 nucleotides.

41.202(a)(3)(b) - Show why the claims interfere within the meaning of § 41.203(a)

An element-by-element analysis of interfering claim 17 of US 6,498,148 and claim 44 of US 09/337,584 is provided as follows:

1.

Claim 17 of US 6,498,148	Claim 44 of US 09/337,584
A method for treating asthma, comprising:	A method for treating asthma in a subject, comprising

Each claim is directed to a method for treating asthma.

Therefore, to the extent that the preamble of a claim is a limitation of a claim, claim 17 anticipates this element of claim 44, and claim 44 anticipates this element of claim 17.

2.

administering to a mammal sensitized to an asthma-stimulating antigen	administering to an asthmatic subject

Claim 17 requires administration to a "mammal sensitized to an asthma stimulating antigen." Claim 44 requires administration to an asthmatic subject.

Claim 17 anticipates or renders obvious this element of Claim 44. Claim 17 is directed to treating asthma. Administration of drug is in an amount effective to treat asthma. "Mammals sensitized to an asthma stimulating antigen" obviously include asthmatic subjects. Claim 17 clearly contemplates treating an asthmatic subject.

Claim 44 renders obvious this element of claim 17. Asthmatic subjects (claim 44) include mammals (claim 17). Treating mammals, and especially humans, is the clear and obvious objective of asthma therapy. Asthmatic subjects (claim 44) also are necessarily sensitized to an asthma-stimulating antigen (claim 17). Asthma is defined in US 09/337,584 as an acquired hypersensitivity to an antigen. (Allergy, including asthma, is an "acquired hypersensitivity to a substance (allergen)". US 09/337,584, page 13, lines 26-28).

3.

an immunostimulatory polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the sequence 5'-cytosine-guanine-3',	an immunostimulatory nucleic acid, having a sequence including at least the following formula: 5' X_1 X_2CGX_3 X_4 3' wherein C is unmethylated, wherein X_1X_2 and X_3X_4 are nucleotides,

Each claim requires an immunostimulatory polynucleotide comprising a CG dinucleotide sequence.

Claim 17 renders obvious this element of claim 44. Claim 17 of US 6,498,148 does not explicitly require that the cytosine nucleotide of the sequence 5'-cytosine-guanine-3' be unmethylated, as in claim 44 of US 09/337,584. However, at the time that US 6,498,148 was filed, it was well known in the art that unmethylated cytosines (C) in CG sequences are important for immune stimulatory activity. In particular Krieg et al., Nature 374:546-549, 1995 (hereinafter "Krieg") teaches that immunostimulatory activity of nucleic acids containing a CpG sequence *depends* on the C being unmethylated. The same teaching is contained in prior art issued patent US 6,194,388. The importance of an unmethylated C was also acknowledged in papers published by the patentees of US 6,498,148 (see, e.g., Sato et al., Science 273: 352-354, 1996). The importance of an unmethylated CG sequence further was acknowledged in US 6,498,148 itself, which states at Col. 8, lines 31-33 that the ISS may include an unmethylated CG sequence. In addition, in Interference 105,171, the Assignee of US 6,498,148 admitted, in referring to "Krieg", that "Krieg et al. specifically discusses the importance of unmethylated CpG dinucleotides". (Opposition 8, page 10, Material Fact 35). Therefore, claim 17 of US 6,498,148 describes a genus (methylated or unmethylated C) which renders obvious the subgenus (unmethylated) of claim 44.

Claim 17 of US 6,498,148 also does not recite the specific sequence recited in claim 44 of US 09/337,584. Claim 17, however, renders this element of claim 44 obvious. Claim 17 requires a polynucleotide sequence having at least 6 nucleotides and comprising 5'CG3'. The formula recited in claim 44 of US 09/337,584 also requires a polynucleotide sequence having at

least 6 nucleotides, and comprising 5'CG3'. The limitation of claim 17 is slightly broader than the corresponding limitation of claim 44 because the location of the CG in the polynucleotide is not restricted in claim 17, while in claim 44 the CG nucleotides must be flanked by at least two nucleotides on either side i.e., 5'-$X_1X_2CGX_3X_4$-3') This limitation of claim 44 is obvious over claim 17 in view of prior art patent US 6,194,388, which describes a formula similar to that of claim 44 and also in view of Krieg which describes nucleotides with flanking bases.

Therefore, claim 44 anticipates this element of claim 17 because a subgenus anticipates a genus. Claim 17 renders obvious this element of claim 44 because it would have been obvious, beginning with the immunostimulatory sequence of claim 17 (which has at least six nucleotides and contains a CG), to select a sequence where the CG is unmethylated and is flanked on either side by at least two nucleotides.

4.

wherein the immunostimulatory polynucleotide does not comprise a nucleotide sequence encoding the antigen,	

Claim 17 requires that the polynucleotide "not" encode "the antigen". Claim 44 is silent with respect to whether the oligonucleotide encodes any antigen.

Claim 17 anticipates this element of claim 44 because claim 17 falls completely within this element of claim 44.

Claim 44 anticipates or renders obvious this element of claim 17 because (i) the prior art discloses that the immunostimulatory nucleic acid need not code for any antigen at all, let alone "the antigen", to have its immunostimulatory effect and/or (ii) an oligonucleotide of 8-100 nucleic acids in length cannot "encode" any antigen (including "the antigen").

The oligonucleotide of claim 44 is limited to a length of 8-100 nucleotides, and one of ordinary skill in the art would have interpreted claim 44 as "not" encoding any antigen, let alone "the antigen". "The prior art, including US 6,194,388 and Krieg," teach that immunostimulation

by CG containing polynucleotides is independent of "coding", and the immunostimulatory polynucleotides exemplified in this prior art are non-coding of any antigen. It is inherent or, at a minimum, it would have been obvious, that the oligonucleotide could be non-coding of any antigen.

Additionally, the reasonable interpretation of the limitation of claim 17 is that the words "do not encode" mean "do not produce" or "do not direct the expression of". It is not the presence of the sequence that is to be avoided, but rather the presence of the antigen. The claim is directed to monotherapy, that is, immune stimulation without an antigen. Claim 44 describes an oligonucleotide 8-100 nucleotides in length, which is too short to be capable of directing the expression of the antigen.

Claim 17 anticipates this element of claim 44 because claim 17 is either the same as or falls completely within this element of claim 44.

5.

and wherein the immunostimulatory polynucleotide is administered without the antigen, including without a polynucleotide encoding the antigen,	

Claim 17 calls for administration without the antigen. Claim 44 is silent with respect to whether an antigen is administered. Claim 44 embraces administering with or without an antigen.

Claim 17 anticipates this element of claim 44 of US 09/337,584. Claim 17 (without the antigen) falls completely within this element of claim 44 (with or without antigen).

Claim 44 would have rendered obvious this element of claim 17. At the time that US 6,498,148 was filed, it was known that CpG oligonucleotides given without any

antigen to mammals were able to stimulate/modulate the immune system, induce particular cytokine production, and treat various conditions (e.g., see US 6,194,388 and "Krieg"). The ability of CpG oligonucleotides given without any antigen to stimulate cytokines, thereby causing a Th2 → Th1 shift, in particular, is disclosed in US 6,207,646, the grandparent of the instant application Thus, taking claim 44 as prior art, claim 17 of US 6,498,148 would have been obvious because one of ordinary skill in the art would have been motivated to administer CpG without antigen due to the knowledge in the art that antigen administration was unnecessary for obtaining the desired immune effects, including the desired cytokine profiles. The person of skill in the art would have had a reasonable expectation of success in doing so for the same reasons.

6.

and in an amount sufficient to treat asthma.	an effective amount for treating asthma in the subject of

These limitations are essentially identical; each anticipates the other.

7.

[Claim 17]: The method of claim 1, wherein the ISS is at least six nucleotides in length.	wherein the nucleic acid has a length of 8 to 100 nucleotides.

Taking claim 44 as prior art, claim 17 is anticipated because an oligonucleotide of at least 6 nucleotides is a genus that is anticipated by the sub genus (8-100) recited in claim 44.

Taking claim 17 as prior art, claim 44 would have been obvious based on the knowledge in the art that oligonucleotides within the stated size range were useful in immunostimulation, e.g., see Krieg, US 6,194,388 or US 6,207,646.

Summary of interference between the claims within the meaning of § 41.203(a)

Elements 1, 2, 3 and 6 of the two claims are essentially identical. Claim 17 anticipates elements 4 and 5 of claim 44. Claim 44 anticipates or renders obvious elements 4 and 5 of claim

17. Claim 44 anticipates element 7 of claim 17. Claim 17 renders obvious element 7 of claim 44.

41.202(a)(4) - Explain why applicant will prevail on priority

Applicant's claimed invention is disclosed and supported in priority filings at least as early as US 08/738,652, now 6,207,646, filed on October 30, 1996. US Patent 6,498,148 was filed on January 21, 1999 and has an alleged earliest effective filing date of September 5, 1997. Therefore, Applicant has a constructive reduction to practice more than 10 months prior to the filing date of US 6,498,148.

41.202(a)(5) - Claim chart showing the written description for each claim, if claim added or amended to provoke interference.

Not applicable.

41.202(a)(6) - Chart showing where the disclosure provides a constructive reduction to practice within the scope of the interfering subject matter.

While Applicant has an actual reduction to practice for the claimed invention to the extent it embraces administering an immunostimulatory nucleic acid both with and without an antigen, a constructive reduction to practice for the method in which and effective amount of an immunostimulatory nucleic acid is administered without antigen is shown in the chart below.

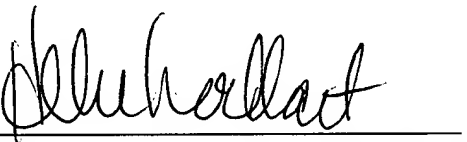
Claim 44 of US 09/337,584	Constructive reduction to practice
A method for treating asthma in a subject, comprising	**Page 9, lines 8-12:** "Furthermore, by redirecting a subject's immune response from Th2 to Th1, the claimed nucleic acid sequences can be used to treat or prevent an asthmatic disorder. In addition, the claimed nucleic acid molecules can be administered to a subject in conjunction with a particular allergen as a type of desensitization therapy to treat or prevent the occurrence of an allergic reaction associated with an asthmatic disorder." **Example 12:, first paragraph, spanning pages 63-64**: "6-8 week old C56BL/6 mice (from The Jackson Laboratory, Bar Harbor, ME) were immunized with 5,000 Schistosoma mansoni eggs by intraperitoneal (i.p.) injection on days 0 and 7. Schistosoma mansoni eggs contain an antigen (Schistosoma mansoni egg antigen (SEA)) that induces a Th2 immune response (*e.g.* production of IgE antibody). IgE antibody production is known to be an important cause of asthma." **Paragraph spanning pages 54-55**: "As described in detail in the following Example 12, oligonucleotides containing an unmethylated CpG motif (i.e. TCCATGACGTTCCTGACGTT; SEQ ID NO. 10), but not a control oligonucleotide (TCCATGAGCTTCCTGAGTCT; SEQ ID NO 11) prevented the development of an inflammatory cellular infiltrate and eosinophilia in a murine model of asthma. Furthermore, the suppression of eosinophilic inflammation was associated with a suppression of a Th2 response and induction of a Th1 response."
administering to an asthmatic subject an effective amount for treating asthma in the subject of	**Page 54, lines 25-27**: An "effective amount" for treating asthma can be that amount useful for redirecting a Th2 type of immune response that is associated with asthma to a Th1 type of response.

	Example 12, page 64, lines 3-4: "The immunized mice were then treated with oligonucleotides (30 μg in 200 μl saline by i.p. injection)...." **Fig. 14 description, spanning pages 64-65:** "Figure 14 shows that administration of an oligonucleotide containing an unmethylated CpG motif can actually redirect the cytokine response of the lung to production of Il-12, indicating the Th1 type of immune response."
an immunostimulatory nucleic acid, having a sequence including at least the following formula: 5' X_1 X_2CGX_3 X_4 3' wherein C is unmethylated, wherein X_1X_2 and X_3X_4 are nucleotides, wherein the nucleic acid has a length of 8 to 100 nucleotides.	**Example 12, page 64, lines 4-5:** "which ... contained an unmethylated CpG motif (*i.e.*, TCCATGACGTTCCTGACGTT; SEQ ID NO.10)..." **Page 53, lines 25-26**: "Nucleic acids containing unmethylated CpG motifs may also have significant therapeutic utility in the treatment of asthma."

CONCLUSION

If any part of the foregoing is unclear, the Examiner is respectfully requested to call the Applicant's attorney at the telephone number listed below. If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
Arthur M. Krieg et al., Applicant

By: 

Helen C. Lockhart, Ph.D., Reg. No.: 39,248
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
Telephone: (617) 646-8000

Docket No.: C1039.70020US00
Date: August 25, 2006
xnddx